

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in this application.

The following amendments do not constitute an admission regarding the patentability of the amended subject matter and should not be so construed. Amendments to the claims were made for purposes of more clearly stating the claimed subject matter and do not add new matter or alter the scope of the claims.

### **Listing of Claims**

1. (Currently amended) A method for inferring a network relationship between genes, comprising:
  - (a) providing a quantitative time course data library for a set of genes of an organism, said library including expression results based on time course of expression of each gene in said set of genes,
    - (a1) quantifying an average effect and measure of variability of each time point on each other of said genes;
  - (b) creating a sparse matrix from said library, said matrix having zero coefficients removed therefrom;
  - (c) generating a set of linear differential equations from said matrix; ~~and~~
  - (d) solving said set of equations thereby inferring to produce said network relationship; ~~and~~
    - (d1) mapping said network relationship.
2. (Original) The method of claim 1, wherein said zero coefficients are identified using Akaike's Information Criterion (AIC).
3. (Original) The method of claim 1, wherein said differential equation is

$$\frac{d}{dt}x(t) = \underline{A} \bullet x(t),$$

in which the vector  $\underline{x}(t)$  contains the amount of expressed cDNA as a function of time, and the matrix  $\underline{\Lambda}$  is a constant with units second<sup>-1</sup>.

4. (Original) The method of claim 1, wherein said matrix contains elements  $\Lambda_{ij}$ , wherein  $\Lambda_{ij}$  represents the effect of gene  $j$  on gene  $i$ , and wherein  $[\Lambda_{ij}]^{-1}$  represents the reaction time for said effect of gene  $j$  on gene  $i$ .

5. (Currently amended) The method of claim 1, wherein said differential equation solved is

$$\underline{x}(t) = \exp[\underline{\Lambda}t] \cdot \underline{x}_0 \cdot \vec{e}_t$$

6. (Currently amended) The method of claim 5, wherein said exponent  $\underline{\Lambda}t$  ( $\exp(\underline{\Lambda})$ ) is solved using the formula:

$$\exp(\underline{\Lambda}) = \sum_{i=0}^{\infty} \frac{1}{i!} \underline{\Lambda}^i$$

7. (Original) The method of claim 1, wherein said differential equation is estimated by solving the difference equation:

$$\frac{\Delta x}{\Delta t} = \underline{\Lambda} \cdot \underline{x}$$

8. (Original) The method of claim 1, wherein said sparse matrix further comprises an error estimated using, the formula:

$$\underline{x}(t + \Delta t) - \underline{x}(t) = \Delta t \cdot \underline{\Lambda} \cdot \underline{x}(t) + \underline{\varepsilon}(t)$$

9. (Original) The method of claim 8, wherein said error has a normal distribution independent of time according to the formula:

$$f(\underline{\varepsilon}(t); \sigma^2) = \left( \frac{1}{\sqrt{2\pi\sigma^2}} \right)^m \exp \left\{ -\frac{\underline{\varepsilon}(t)^T \cdot \underline{\varepsilon}(t)}{2\sigma^2} \right\},$$

wherein standard deviation  $\sigma$  is equal for each of said genes at all times.

10. (Currently amended) The method of claim 1, wherein the a maximum likelihood estimate of the variance  $\sigma^2$  is determined by maximizing the log-likelihood function with respect to  $\sigma^2$  using the formula:

$$\hat{\sigma}^2 = \frac{1}{nm} \sum_{i=1}^n \hat{\underline{\varepsilon}}_i^T \cdot \hat{\underline{\varepsilon}}_i.$$

11. (Original) The method of claim 10, wherein said variance  $\sigma^2$  is determined using the formula:

$$\hat{\sigma}^2 = \frac{1}{nm} \sum_{i=1}^n \left[ (\underline{x}_i^T - \underline{x}_{i-1}^T) \cdot (\underline{x}_i - \underline{x}_{i-1}) + (t_i - t_{i-1})^2 \underline{x}_{i-1}^T \cdot \underline{\Delta}^T \cdot \underline{\Delta} \cdot \underline{x}_{i-1} - 2(\underline{x}_i^T - (t_i - t_{i-1})\underline{x}_{i-1}^T) \cdot \underline{\Delta} \cdot \underline{x}_{i-1} \right].$$

12. (Currently amended) The method of claim 2, wherein said AIC is minimized using the formula:

$$AIC = 2 \cdot \left[ \frac{\log - \text{likelihood of the}}{\text{estimated model}} \right] + 2 \cdot \left[ \frac{\text{number of estimated}}{\text{parameters}} \right] \quad (16)$$

13. (Currently amended) The method of claim 1, wherein a mask  $\underline{\hat{M}}$  is used to set matrix elements of  $\underline{\hat{\Lambda}}$  equal to zero using the formula:

$$\underline{\hat{\Lambda}}' = \underline{\hat{M}} \circ \underline{\hat{\Lambda}},$$

where  $\odot$  denotes an element-wise product, and mask  $\mathbb{M}$  is a matrix whose elements are either one or zero.

14. (Original) The method of claim 13, wherein matrix elements are set to zero by applying a mask  $\mathbb{M}$  produced by minimizing the formula:

$$\text{if } M_{ij} = 1 : \left[ \hat{\underline{\underline{A}}} \cdot \underline{\underline{A}} \right]_{ij} = B_{ij};$$

$$\text{if } M_{ij} = 0 : \hat{\underline{\underline{A}}} \cdot \underline{\underline{A}}_{ij} = 0;$$

thereby yielding the maximum likelihood estimate  $\hat{\underline{\underline{A}}}'$ .

15. (Original) The method of claim 2, wherein said AIC is minimized according to the formula:

$$AIC = nm \ln \left[ 2\pi\hat{\sigma}^2 \right] + nm + 2 \cdot \left( 1 + \left[ \text{sum of the maselements } M_{ij} \right] \right).$$

16. (Original) The method of claim 13, wherein said mask  $\mathbb{M}$  is selected to minimize AIC calculated using the formula:

$$AIC = nm \ln \left[ 2\pi\hat{\sigma}^2 \right] + nm + 2 \cdot \left( 1 + \left[ \text{sum of the maselements } M_{ij} \right] \right).$$

17. (Original) A medium containing one or more results of network relationships between genes calculated using a method of claim 1 stored thereon.